PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION See Form PCT/IPEA/416	
13132PCHK		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/FI 2003/000241	28.03.2003	28.03.2002
International Patent Classification (IPC) or national classification and IPC		
A61K 9/72, A61K 47/00, A61J 3/02		
Applicant		
Focus Inhalation OY et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 3 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
27.10.2003	06.08.2004
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. +46 8 667 72 88	Authorized officer Carolina Gómez Lagerlöf/BS Telephone No. +46 8 782 25 00

Form PCT/IPEA/409 (cover sheet) (January 2004)

CORRECTED

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

Interna[redacted] application No.
PCT/FI 2003/000241

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))
☐ publication of the international application (under Rule 12.4)
☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

☐ the international application as originally filed/furnished

☒ the ~~description~~:

pages 1-16 as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☒ the claims:

pages _____ as originally filed/furnished
pages* _____ as amended (together with any statement) under Article 19
pages* 1-3 received by this Authority on 2004-03-29
pages* _____ received by this Authority on _____

☒ the drawings:

pages 1-6 as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/FI 2003/000241

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-19	YES
	Claims		NO
Inventive step (IS)	Claims	1-19	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-19	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The following documents were cited in the International Search Report:

D1: WO 99/9934778 A1
D2: Iida K et al; "Evaluation of Flow Properties of Dry Powder Inhalation of Salbutamol Sulfate with Lactose Carrier"; Chem. Pharm. Bull. 49(10) 1326-1330 (2001)
D3: WO 02/07705 A1

The problem the present invention aims to solve is to improve the stability and flow properties of carrier particles for an inhalation powder. This is achieved by abrading the particles by suspending them in a liquid medium in which the carrier is essentially insoluble and then removing the liquid medium.

The document D1 describes a method for preparing a powder preparation containing an active agent and optionally for example a carrier. According to this method the particles are suspended in a suspending agent in which they are essentially insoluble and the suspending agent is then evaporated. The achieved particles are use in inhalation powder and have improved stability. In example 2 salbutamol sulphate and lactose are suspended in n-hexane and stirred for some hours. The experiment results in a well-flowing powder ready for formulation.

D2 discusses the properties of carrier powder for inhalation and concludes that surface-treated carrier particles have improved flow and packing properties. Lactose particles are mixed and stirred with aqueous ethanol solution whereby protuberances are dissolved.

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V

D3 discloses spherical carrier particles without amorphous material for use in inhalation formulations.

None of the above mentioned documents show a method where the carrier is abraded suspended in a liquid medium.
Thus, the documents show the general state of the art.

Claims 1-19 are considered to fulfil the requirements of novelty, inventive step and industrial applicability.

Claims

1. Method for treating a particulate carrier for an inhalation powder improving stability and flow properties of the carrier, **characterized** in that carrier is abraded suspended in a liquid medium into which the carrier is essentially insoluble using an effect below that required for crushing the carrier particles, the liquid medium is removed and the carrier recovered.

2. Method according to claim 1, **characterized** in that the carrier is abraded with a mixing device.

3. Method according to claim 1 or 2, **characterized** in that the rotation speed of the mixing device is lowered during the treatment.

4. Method according to any of claim 1 to 3, **characterized** in that the carrier suspension is cooled and recirculated to the mixer.

5. A method according to any of the proceeding claims, **characterized** in that the suspension is recirculated through a filter.

6. A method according to claim 5, **characterized** in that a certain desired size range or ranges are recirculated to the mixing device.

7. A method according to any of the proceeding claims, **characterized** in that said media is a hydrocarbon, perfluorinated ether, fluorinated ether, perfluorinated hydrocarbon, fluorinated hydrocarbon, methanol, ethanol or any other alcohol or hydrocarbon.

8. A method according to any of the proceeding claims, **characterized** in that said carrier after filtration is used undried for formulation.

9. A method according to any of the proceeding claims, **characterized** in that said carrier is dried after filtration and stored for future used.

10. A method according to any of the proceeding claims, **characterized** in that the abraded carrier is at least partly covered particles smaller in size than said carrier.

11. A method according to claim 10, **characterized** in that the abraded carrier and the small sized particles are of the same material.

12. A method according to any of the proceeding claims, **characterized** in that the carrier to be abraded is lactose or a monohydrate thereof, glucose, mannitol, trehalose, sucrose, any other sugar, polysaccharide or any other compound used as a carrier.

13. Carrier for an inhalation powder, which carrier is stable and possesses good flowing properties, **characterized** in that the carrier is abraded suspended in a liquid medium, in which said carrier is essentially insoluble, and using an effect below that required for crushing the carrier particles,

14. Carrier according to claim 13, **characterized** in that that the carrier is abraded with a mixing device.

15. Carrier according to claim 13 or 14, **characterized** in that the carrier is filtrated and used for formulation undried or dried and stored for future use.

16. Carrier according to any of the claims 13 - 15, **characterised** in that the filtrated carrier contains more than one main range of particle sizes of abraded carrier.

17. Carrier according to any of the proceeding claims, **characterized** in that the carrier to be abraded is lactose or a monohydrate thereof, glucose, mannitol, trehalose, sucrose, any other sugar, polysaccharide or any other compound used as a carrier.

18. Preparation for inhalation purposes comprising an active agent, a carrier and optional excipients used in inhalable preparation, **characterized** in that at least a part of the carrier used is abraded suspended in a liquid medium, in which the carrier in essentially insoluble.

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19. A preparation according to claim 18, **characterized** in that carrier contains more than one main range of particle sizes.